

REMARKS

Claims 4-7, 34, 37, 38, 46, 49-51, 53-63, 65, 72, 74-78, 94-96, 100, and 104 are pending in the present application. Claim 34 is amended to provide further clarity. Claim 100 is canceled. Claim 105 is added. Claim 105 finds support throughout the application. All claim amendments are made without prejudice and do not represent acquiescence in any ground of rejection. Applicants reserve the right to pursue the subject matter of claim 100 in continuing applications.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 100 is rejected under 35 U.S.C. § 112 as non-enabled. Although Applicants do not agree, in order to expedite prosecution, Applicants have canceled claim 100. Applicants respectfully request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 4-7, 34, 37, 38, 46, 49-51, 53-63, 65, 72, 74-78, 94-96, 100, and 104 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Elbashir *et al.*, The EMBO Journal, 2001, Vol. 20, No. 23, pages 6877-6888 (the Elbashir reference); Fosnaugh *et al.*, US 2003/0143732 (the Fosnaugh reference); and Morrissey *et al.*, US 2003/0206887 (the Morrissey reference) in view of the combined teachings of Arnold *et al.*, US 6,262,036 (the Arnold reference); Damha *et al.*, US 2005/0142535 (the Damha reference); and McKay *et al.*, US 6,133,246 (the McKay reference). Applicants respectfully traverse.

In assessing whether subject matter would have been non-obvious under section 103, examiners are to apply the test for patentability set forth by the Supreme Court in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). MPEP § 2141. In that case, the Court stated:

Under §103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but

unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy. . .

Graham, 383 U.S. at 17-18.

Objective evidence or secondary considerations such as unexpected results, commercial success, long-felt need, failure of others, copying by others, licensing, and skepticism of experts are relevant to the issue of obviousness and must be considered in every case in which they are present. MPEP § 2141. When evidence of any of these secondary considerations is submitted, the examiner must evaluate the evidence. MPEP § 2141.

The present claims are directed to a composition comprising two oligomeric compounds wherein at least one of the oligomeric compounds has alternating 2' β -D-deoxyribonucleosides with 2'-modified nucleosides. Before the advent of the present invention, it could not have been expected that a double stranded composition comprising an oligomeric compound having such a motif would be active. Neither the primary references cited in the Action, the Elbashir, Fosnaugh, and Morrissey references, nor the secondary references, the Arnold, Damha, and McKay references, teach a motif of alternating 2' β -D-deoxyribonucleosides with 2'-modified nucleosides in a double stranded composition. The Action appears to be rejecting the claims on the basis that the skilled artisan would expect that any one of the many known motifs for use with antisense oligonucleotides could be adapted for use with siRNA duplexes, and result in active compositions. The references cited in the Action, however, provide *objective* evidence that the skilled artisan *could not* have reasonably expected that the strands of a siRNA duplex could be modified in such a manner and result in an active composition. For example, example 34 of the Arnold reference describes *2'-O-methyl substitutions on all of the residues in a repeated sequence* of an antisense oligonucleotide and reports a dramatic *improvement* in binding stability. In the Elbashir reference, however, it is reported in the abstract that *substitution of one or both siRNA strands by 2'-deoxy or 2'-O-methyl oligonucleotides abolished activity*. Clearly, the Elbashir reference, combined with the Arnold reference, demonstrates that, contrary to the allegations presented in the Action, it could not have been reasonably expected that any

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motif, and, in particular, an alternating 2' β -D-deoxyribonucleoside with 2'-modified nucleoside motif, would be desirable. The Action simply fails to provide any reason why a person of ordinary skill would use an alternating 2' β -D-deoxyribonucleoside with 2'-modified nucleoside motif as provided in the claims, particularly given the combined teachings of the Arnold and Elbashir references. Withdrawal of the rejection is respectfully requested in view of the objective evidence of nonobviousness presented herein.

Double Patenting

Claims 4-7, 34, 37, 38, 46, 49-51, 53-63, 65, 72, 74-78, 94-96, 100, and 104 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 36, 40, 44, 46-49, 52-64, 74-80, 93, 98-100, and 104 of copending Application No. 10/860,265 or claims 1-24 of copending Application No. 11/054,848. Applicants respectfully request that this rejection be deferred pending some identification of allowable subject matter, as it likely can be readily resolved (depending upon the subject matter ultimately allowed) through the filing of a suitable terminal disclaimer.

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Applicants respectfully submit that the present application is in condition for allowance. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided. Favorable consideration and an early notice of allowance are respectfully requested.

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